PATENT
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Hans DECKMYN et al.	Art Unit:	1644
Serial No.:	10/049,868	Examiner:	Maher M. Haddad
Filed:	June 4, 2002	Customer No.:	21559
Title:	CELL LINES, LIGANDS AND ANTIBODY FRAGMENTS FOR USE IN PHARMACEUTICAL COMPOSITIONS FOR PREVENTING AND TREATING HAEMOSTASIS DISORDERS		

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. 1.132 OF DR. HANS DECKMYM

1. I am a named inventor on the above-referenced patent application.

2. I have read the Office Action mailed November 4, 2004, and I have considered the Office's remarks regarding the teachings of the specification with respect to the broad scope of the present claims. In my opinion, these concerns are unwarranted.

3. As evidence of the enabling nature of the specification, I note that an additional monovalent antibody fragment which binds *in vivo* to platelet glycoprotein GP1b has been produced using standard methods known at the time the above-referenced application was filed.

4. As explained below, I present additional data demonstrating that a classical antibody against GP1b induces thrombocytopenia, while a monovalent antibody fragment, such as an Fab fragment of the antibody against GP1b fails to induce thrombocytopenia.

5. Our experiments were performed as follows.[1] Briefly, male Wistar rats were injected intravenously with either complete IgG or Fab fragments of RPM15, an inhibitory monoclonal antibody against rat GP1b. Blood samples were taken before and at different time points after injection. The number of platelets in these blood samples is indicative of the occurrence of thrombocytopenia. The results are provided in the accompanying Figure 1, in which panel A demonstrates the effect of complete RPM15 IgG on platelet number and panel B illustrates the effect of monovalent RMP15 Fab fragments on platelet number. These results demonstrated that the Fab fragment has no effect on platelet number thus does not cause thrombocytopenia *in vivo*.

6. In addition, the results demonstrate that a monovalent antibody fragment of an inhibitory GP1b antibody does not cause thrombocytopenia *in vivo* and is thus suitable for use as a pharmaceutical composition.

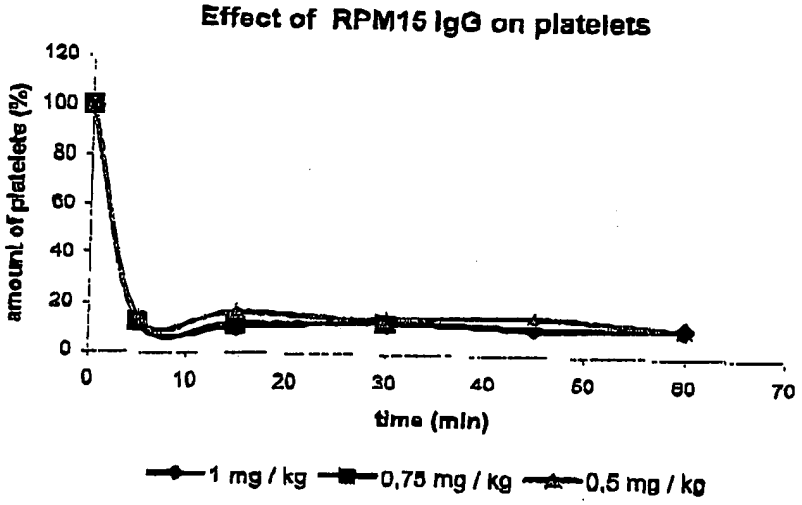
[1] A detailed description of the experiment is attached as appendix a.

7. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

Date: 4-3-2005

Dr. Hana Deckmyn

A



B

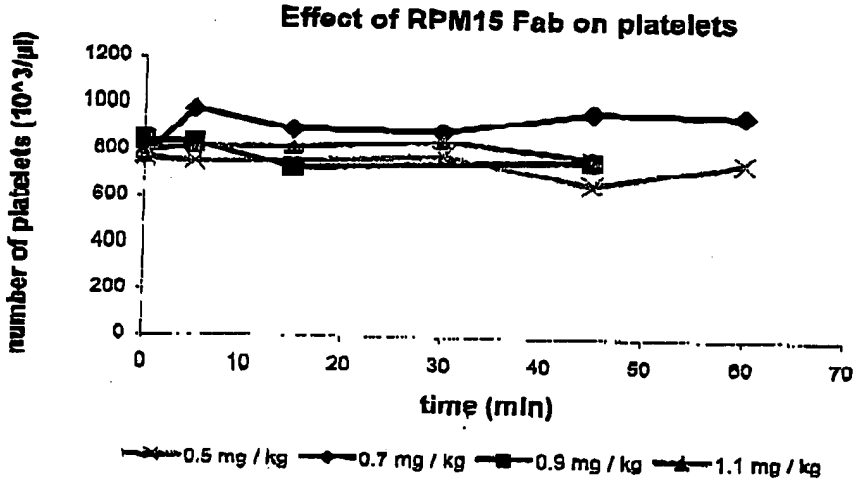


Figure 1: Effect of complete anti-GP1b IgG and monovalent antibody fragments thereof on thrombocytopenia

Appendix a: detailed description of the experiment

Wildtype male Wistar rats were sedated with Nembutal® (1mg/kg). A butterfly-catheter was placed in the vena femoralis. Different concentrations of RPM15 (an inhibitory antibody to rat GP1b) were prepared by dilution in PBS to a final volume of 500µl. Solutions of 0.5, 0.75, and 1 mg/kg of complete IgG and 0.5, 0.7, 0.9 and 1.1 mg/kg of Fab fragments of RPM15 were prepared. These solutions were administered intravenously in the vena femoralis through the catheter.

Before injection of the antibody or antibody fragments and at different time points after injection blood samples were taken by collecting 450µl blood through the catheter in a syringe containing 50µl citrate. Directly after taking the blood sample the number of platelets was determined using the Cell-dyn® 1300 cell-counter (Abott).

Five minutes after injection of complete RPM15 IgG, a clear decrease of number of platelets was observed for all concentrations (decrease of 85%), which lasted for at least one hour (total time of observation). The administration of RPM15 Fab fragments did not induce thrombocytopenia at any concentrations during the first hour after injection.